PATENT Case: 027664 (formerly 01288)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF Steven MacLeod	GROUP ART UNIT: 3761
SERIAL NO: 10/644,516	EXAMINER: Leslie Deak
FILED: 08/20/2003	DATE: 05/07/2007

TITLE: INJECTABLE PHARMACEUTICAL SUSPENSION IN A TWO-CHAMBER VIAL

May 7, 2007

AMENDED APPEAL BRIEF

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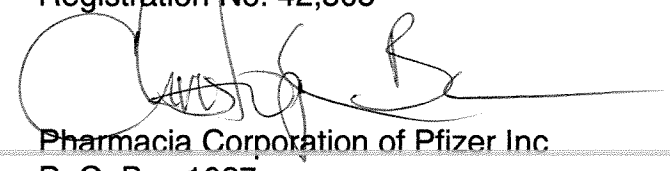

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TABLE OF CONTENTS

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AMENDED APPEAL BRIEF

This is an appeal from the final rejection of the above-identified application made in the Office action mailed March 16, 2006 and in response to the Notification of Non-Compliant Appeal Brief mailed March 09, 2007. A one month extension of time under 37 CFR 1.136 is hereby requested.

I. Real Party In Interest

The real party in interest is Pharmacia Corporation, owner of 100 percent interest in the pending application. Pharmacia Corporation is a wholly owned subsidiary of Pfizer Inc., a corporation of the State of Delaware.

II. Related Appeals and Interferences

No other appeals or interferences are known to Appellant, which will directly affect or be directly affected by or have a bearing on the Board's decision in the present appeal.

III. Status of Claims

The above captioned application was originally filed with twenty three claims. Claim 4 was canceled in the response filed January 20, 2006. Claims 1-3 & 5-23 are pending. Claims 1-3 & 5-23 are under appeal.

IV. Status of Amendments

An Amendment after final rejection was filed August 11, 2006, but no amendments were made to the claims, therefore there are no outstanding amendments to the claims.

V. Summary of the claimed subject matter

The invention of claims 1-3 is directed to a plural compartment mixing vial wherein a center plug placed between two compartments for temporarily isolating a liquid-containing compartment from a gaseous medium.

The four claimed elements of claim 1 are:

(a) a first chamber **14** that is substantially filled with a parenterally deliverable aqueous suspension that comprises (i) an aqueous medium; (ii) a drug in solid particulate form in a therapeutically effective amount suspended in the medium; and (iii) one or more wetting and/or suspending agents in an amount effective to provide controlled flocculation of the drug, at least one ingredient of the formulation being susceptible to oxidative degradation; (lines 2-7 of [0012] p. 3; lines 3 & 4 of [0021] p. 5; line 7 of [0024] p. 6; lines 6 & 7 of [0025] p. 6; and "14" of Figure 2)

(b) a second chamber **13** that is substantially empty but for a gaseous medium; (lines 7 & 8 of [0012] p. 3; lines 3 & 4 of [0021] p. 5; lines 6 & 7 of [0024] p. 6; lines 7 & 8 of [0025] p. 6; and "13" of Figure 2)

(c) a septum **17** separating the first and second chambers and impermeable to the gaseous medium; and (lines 8 & 9 of [0012] p. 3; lines 4 & 5 of [0021] p. 5; lines 3 & 4 and lines 8 & 9 of [0024] p. 6; and "17" of Figure 2)

(d) an actuating means effective to bring the aqueous suspension and the gaseous medium into contact by breach of the septum such that the gaseous medium acts as an effective headspace for agitation of the formulation. (line 9 {p. 3} to line 2 {p. 4} of [0012]; line 2 & 3 of [0027] p. 7)

The present claim differs from the prior art in the selection of a gas impermeable septum **17** (lines 8 & 9 of [0012] p. 3; lines 4 & 5 of [0021] p. 5; lines 3 & 4 and lines 8 & 9 of [0024] p. 6; and "17" of Figure 2) separating an aqueous suspension comprising i) an aqueous medium; ii) a drug in solid particulate form; iii) a wetting and/or suspending agent – at least one of the ingredients being susceptible to oxidation (lines 2-7 of [0012] p. 3); from a gaseous compartment **13** (lines 7 & 8 of [0012] p. 3; lines 3 & 4 of [0021] p. 5; lines 6 & 7 of [0024] p. 6; lines 7 & 8 of [0025] p. 6; and "13" of Figure 2) compared to a moisture barrier separating an aqueous compartment form a lyophilized component. In the present invention a multiple chamber vial configuration was discovered where a drug substance in solid particulate form could be stored in an aqueous medium providing controlled flocculation (line 2 of [0022] p. 5) and eliminating the headspace in the compartment to prevent oxidation of an ingredient in the formulation (lines 1 & 2 of [0022] p. 5) and proving a second compartment comprising a gaseous component **13** (lines 7 & 8 of [0012] p. 3; lines 3 & 4 of [0021] p. 5; lines 6 & 7 of [0024] p. 6; lines 7 & 8 of [0025] p. 6; and "13" of Figure 2) separated from the aqueous compartment **14**

(lines 2-7 of [0012] p. 3; lines 3 & 4 of [0021] p. 5; line 7 of [0024] p. 6; lines 6 & 7 of [0025] p. 6; and "14" of Figure 2) by a gas impermeable septum **17** (lines 8 & 9 of [0012] p. 3; lines 4 & 5 of [0021] p. 5; lines 3 & 4 and lines 8 & 9 of [0024] p. 6; and "17" of Figure 2), which when breached provides a headspace for agitation of the formulation. The multiple problems to be solved were a vial configured to prevent oxidation of an ingredient in one compartment and to create a headspace to allow agitation of the formulation of the drug substance in the form of a controlled flocculant, just prior to administration.

The invention of claim 5 is directed to the invention of Claim 1 wherein the gaseous medium is air (line 8 of [0022] p. 5.

The invention of claims 6-11 is directed to the invention of claim1 wherein the ingredient in the formulation susceptible to oxidative degradation comprises a polyoxyethylene chain ([0013] to [0016] p. 4 & [0060] to [0062] p. 15)

The invention of claim 12 is directed to the invention of claim 1 wherein the drug has low solubility ([0045] p. 10).

The invention of claims 13-16 is directed to the invention of claim 1 wherein the drug is a steroid ([0049] to [0051] p. 12).

The invention of claims 17-23 is directed to the invention on of claim wherein the drug is a medroxyprogesterone (Example 1 to 5 p. 19-25).

VI. Grounds of rejection to be reviewed on appeal

1) Claims 1-3 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,089,432 to Crankshaw et al.

2) Claims 5-23 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,089,432 to Crankshaw et al in view of US 6,481,435 to Hochrainer et al.

VI. Argument

1) Claims 1-3 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,089,432 to Crankshaw et al.

Examiner's Rationale

While the Office concedes that Crankshaw et al. fails to disclose an upper chamber filled with an aqueous medium and a lower chamber filled with a gaseous medium separated by a gas impermeable septum it is argued that the purpose of a two-compartment vial is to provide a stable storage solution wherein two substances, which may include a medication and may be stored completely independently from one another. The Examiner asserts Crankshaw et al. specifically states that the preferred embodiment (upper compartment is filled with a powdered medication and the lower chamber is filled with a solvent) is only one utilization of the invention, thereby contemplating other solutions or compositions in the chambers of the vial.

Applicant's Argument

The Standard for Obviousness

35 U.S.C. § 103(a) states:

> *A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.*

Patentability shall not be negatived by the manner in which the invention was made.

MPEP 2141 describes the standard to be used to assess obviousness:

> Office policy has consistently been to follow Graham v. John Deere Co. in the consideration and determination of obviousness under 35 U.S.C. 103. As quoted above, the four factual inquiries enunciated therein as a background for determining obviousness are briefly as follows:
>
> (A) Determining of the scope and contents of the prior art;
>
> (B) Ascertaining the differences between the prior art and the claims in issue;
>
> (C) Resolving the level of ordinary skill in the pertinent art; and
>
> (D) Evaluating evidence of secondary considerations.

MPEP 2141 (III) states:

> III. CONTENT OF THE PRIOR ART IS DETERMINED AT THE TIME THE INVENTION WAS MADE TO AVOID HINDSIGHT
>
> *Requirement for "at the time the invention was made" is to avoid impermissible hindsight...*
>
> *"It is difficult but necessary that the decision maker forget what he or she has been taught . . . about the claimed invention and cast the mind back to the time the invention was made (often as here many years), to occupy the mind of one skilled in the art who is presented only with the references, and who is normally guided by the then-accepted wisdom in the art." (internal citations omitted).*

Applying the above standard, it is respectfully submitted that a *prima facie* case for obviousness has not been made.

The Vials of the Present Invention

There is no specific direction for the instant claimed vial configuration from the single vial configuration disclosed by Crankshaw et al. that is used with the closure structure claimed by Crankshaw et al. and no teaching of any advantage of the instantly claimed invention. Rather, Crankshaw et al. only makes general statements that modifications are envisioned. The sole example in Crankshaw et al. [1] does not direct the skilled artisan to the configuration claimed in the instant application. Therefore, the claimed invention is not obvious in light of Crankshaw et al. There is simply no direction given in Crankshaw et al. to lead one skilled in the art to make the configuration of the claimed vial.

(A) The Scope and Contents of the Prior Art

The primary object of the Crankshaw et al. disclosure is a "*closure structure including a relatively soft and resiliently flexible stopper and a cap member having a fastening portion mounted upon the neck of a vial and a reduced portion closely surrounding the part of the stopper extending out of the neck of the vial, said reduced portion being movable with the stopper relative to the fastening portion and the neck of the vial.*" [2] Clearly, Crankshaw's invention is the *closure structure* for the vial and the disclosure provides precious little teaching beyond the closure structure. Crankshaw et al. only specifically discloses a single vial configuration wherein an upper compartment is filled with a powdered medication separated by a moisture barrier from the lower chamber filled with a solvent. While Crankshaw et al. may state that this configuration is a particular utilization of the invention [3] and a particular preferred embodiment has been "*disclosed in detail for illustrative purposes, it will be recognized that variations or modifications of the disclosed apparatus, including the rearrangement of parts*" [4], there is **no guidance** as to other contents of the compartments. Crankshaw does not disclose or suggest a gas impermeable septum separating a solid particulate form of a drug substance stored in an aqueous medium providing controlled flocculation and eliminating the head

[1] US 4,089,432 column 3, lines 42-44
[2] US 4,089,432 column 2, lines 4 -11
[3] US 4,089,432 column 3, lines 42-44
[4] US 4,089,432 column 5, lines 54 -59

space in the compartment to prevent oxidation of an ingredient in the formulation from a second compartment comprising a gaseous component.

(B) The Differences Between the Prior Art and the Claims in Issue

In determining the differences between the prior art and the claims, the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. [5] The Examiner's distillation of the present invention down to the mere "gist" or "thrust" of just a two-compartment vial to provide a stable storage solution wherein two substances, which may include a medication, disregards the requirement that the subject matter must be analyzed "as a whole." The problem to be solved is part of the invention as a whole. "[A] patentable invention may lie in the discovery of the source of a problem even though the remedy may be obvious once the source of the problem is identified. This is part of the 'subject matter as a whole' which should always be considered in determining the obviousness of an invention under 35 U.S.C. § 103." [6]

While the presently claimed invention may involve a two component vial and the formulation is more stable upon storage in the claimed configuration, the present invention "as a whole" is more than the mere gist of stable storage in a two chambered vial. The present invention taken as a whole involves the prevention of oxidation of an ingredient in a formulation of a solid particulate form of the drug substance stored in one compartment of a vial as an aqueous medium providing controlled flocculation and eliminating the head space in the compartment separated from a second compartment comprising a gaseous component by a gas impermeable septum, which when breached just prior to administration provides a headspace for agitation of the formulation. The present problem and solution were not envisioned by Crankshaw et al.

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[5] *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983); *Schenck v. Nortron Corp.*, 713 F.2d 782, 218 USPQ 698 (Fed. Cir. 1983).

[6] *In re Sponnoble*, 405 F.2d 578, 585, 160 USPQ 237, 243 (CCPA 1969).

The present invention when taken as a whole is not a reversal of the essential working parts of the vial of Crankshaw et al. Crankshaw et al. et al. provides no alternatives as to the properties of the plug between the compartments other than it serves as a "moisture barrier" or the contents of the compartments; therefore there is nothing specific to reverse. Likewise, the present invention is not an omission of an element and its function in a combination where the remaining elements perform the same function as before. The elimination of the moisture barrier of Crankshaw et al. does not result in a device that functions as a gas impermeable barrier of the present invention. Crankshaw et al. does not teach or contemplate a gas impermeable barrier.

The issue is not whether the art contemplated other combinations but whether the art contemplated the claimed invention. Crankshaw et al. doesn't provide clear blaze marks. It is impermissible to use hindsight based on knowledge from the present application as the bases of an obviousness rejection, the teaching must come from the art itself not from the present disclosure.

(C) The Level of Skill in the Pertinent Art

Even when the level of skill in the art is high any teaching or suggestion to make the claimed combination and a reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure.

Even if it were accepted that Crankshaw's statement, that modifications are envisioned, provides ample motivation to one skilled in the art, a reasonable expectation of success has not been established. The Examiner argues that one skilled in the art would have substituted the lyophilized drug component separated from the aqueous medium by a moisture barrier of Crankshaw et al. with the aqueous drug component and gaseous component of the present invention. However, the Examiner has failed to establish that there was a reasonable expectation of success that the moisture barrier of Crankshaw et al. would effectively serve as a gas impermeable barrier between a gas and a drug containing aqueous medium of the present invention.

(D) Secondary Considerations

Because the applicants believe that there is no *prima facie* case of obviousness present, there is strictly no need to demonstrate secondary considerations. In the interest of completeness, however, applicants point out evidence, present in the specification of the instant application, and shown in the publication of Crankshaw et al. that the instantly claimed configuration is unexpectedly superior to those of Crankshaw et al. Crankshaw et al is completely silent as to the "moisture barrier" acting as a gas impermeable barrier and there is no data showing prevention if oxidation of the formulation by the Crankshaw et al vial. It was unexpectedly shown in Example 1 of the present disclosure that the instant claimed invention significantly reduced polysorbate 80 degradation and pH change (Tables 1 & 2, page 21).

For the foregoing reasons, appellants respectfully submit that Claims 1-3 are patentable under 35 U.S.C. 103(a), over US 4,089,432 to Crankshaw et al. and submit that the rejection of Claims 1-3 under 35 U.S.C. § 103(a), is improper,

2) Claims 5-23 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,089,432 to Crankshaw et al in view of US 6,481,435 to Hochrainer et al.

Examiner's Rationale

The Examiner argues Crankshaw et al. discloses the device substantially as claimed with the exception of the contents and relative formulations of the medicament within the vessel. Hochrainer et al. discloses that steroids such as, for example, clobetasol and meprednisone, among others, are often packaged in two-chambered dispensing vials in suspensions for administration to a patient in various concentrations, since it has been held to be within the general skill of a worker in the art to select a known material on the basis of its suitability for the intended use as a matter of obvious design choice.

2a) Claim 5

Applicant's Argument

For the reasons set forth above and previously presented Crankshaw et al. does not make obvious the invention of claim 5. Crankshaw et al. does not teach or contemplate a gas impermeable barrier. The teachings of Hochrainer et al. do not overcome the shortcomings of Crankshaw et al. The Examiner's argument that Hochrainer et al. discloses steroids in two-chambered dispensing vials in suspensions for administration to a patient, since it has been held to be within the general skill of a worker in the art to select a known material on the basis of its suitability for the intended use as a matter of obvious design choice is not germane to the presently claimed subject because just like Crankshaw et al., Hochrainer et al. is silent with respect to air as the gaseous medium separated by a gas impermeable barrier form the drug and ingredient susceptible to oxidative degradation. Hochrainer et al. adds nothing over Crankshaw et al. with respect to the gaseous medium being air.

2b) Claims 6-11

Applicant's Argument

For the reasons set forth above and previously presented Crankshaw et al. does not make obvious the invention of claims 6-11. Crankshaw et al. does not teach or contemplate a gas impermeable barrier. The teachings of Hochrainer et al. do not overcome the shortcomings of Crankshaw et al. Just like Crankshaw et al., Hochrainer et al. is silent regarding separating the drug formulation from the gaseous medium by a gas impermeable septum to prevent oxidative degradation of a polyoxyethylene chain. Hochrainer et al. adds nothing over Crankshaw et al. with respect to separating the drug formulation from the gaseous medium by a gas impermeable septum to prevent oxidative degradation

of a polyoxyethylene chain. Applicants submit that the Office has failed to establish a *prima facie* case of obviousness.

2c) Claim 12

Applicant's Argument

For the reasons set forth above and previously presented Crankshaw et al. does not make obvious the invention of claim 12. Crankshaw et al. does not teach or contemplate a gas impermeable barrier. The teachings of Hochrainer et al. do not overcome the shortcomings of Crankshaw et al. Just like Crankshaw et al., Hochrainer et al. is silent regarding the drug having low solubility. Hochrainer et al. adds nothing over Crankshaw et al. with respect to drug solubility. Crankshaw et al. in view of Hochrainer et al. do not disclose or suggest the claimed invention as a whole. Applicants submit that the Office has failed to establish a *prima facie* case of obviousness.

2d) Claims 13-16

For the reasons set forth above and previously presented Crankshaw et al. does not make obvious the invention of claim 13-16. The teachings of Hochrainer et al. do not overcome the shortcomings of Crankshaw et al. Hochrainer et al. "*relates to an apparatus comprising a closure-cap and a container in the form of a two-chamber cartridge in which an active ingredient and a solvent can be stored separately until the apparatus is used in a nebuliser, and to a propellant-free active substance concentrate in which the active ingredient is present in highly-concentrated form for storage purposes*" [7] (emphasis added). While Hochrainer et al. may disclose steroids it is silent with respect to separating the drug formulation from a gaseous medium by a gas impermeable septum to prevent oxidative degradation. Crankshaw et al. in view of Hochrainer et al. do

[7] US 6,481,435 column 1, lines 8-14

not disclose or suggest the claimed invention as a whole. Applicants submit that the Office has failed to establish a *prima facie* case of obviousness.

2e) Claims 17-23

For the reasons set forth above and previously presented Crankshaw et al. does not make obvious the invention of claim 17-23. Crankshaw et al. does not teach or contemplate a gas impermeable barrier. Claims 17-23 are not obvious over Crankshaw et al. in view of Hochrainer et al. and patentably distinct because the references do not disclose medroxyprogesterone. Crankshaw et al. in view of Hochrainer et al. do not disclose or suggest the invention as a whole as claimed. Applicants submit that the Office has failed to establish a *prima facie* case of obviousness.

For the foregoing reasons, appellants respectfully submit Claims 5-23 are patentable under 35 U.S.C. 103(a), over US 4,089,432 to Crankshaw et al. in view of US 6,481,435 to Hochrainer et al.

Applicants respectfully request reversal of the rejections of claims 1-3, and 17-23 under 35 U.S.C. § 103(a).

viii. Claims Appendix I

1. An article of manufacture comprising a vial having

(a) a first chamber that is substantially filled with a parenterally deliverable aqueous suspension that comprises (i) an aqueous medium; (ii) a drug in solid particulate form in a therapeutically effective amount suspended in the medium; and (iii) one or more wetting and/or suspending agents in an amount effective to provide controlled flocculation of the drug, at least one ingredient of the formulation being susceptible to oxidative degradation;

(b) a second chamber that is substantially empty but for a gaseous medium;

(c) a septum separating the first and second chambers and impermeable to the gaseous medium; and

(d) actuating means effective to bring the aqueous suspension and the gaseous medium into contact by breach of the septum such that the gaseous medium acts as an effective headspace for agitation of the formulation.

2. The article of Claim 1 wherein the second chamber forms a lower compartment and the first chamber forms an upper compartment; said lower and upper compartments being separated by a constriction wherein the septum in a form of a substantially airtight and watertight plug is engaged; said upper compartment having an annular neck terminating in an open end; said neck having engaged thereon a closure structure comprising (i) a resiliently flexible stopper having a lower sealing portion seated within the neck and an upper protruding portion that projects coaxially beyond the of the neck; said stopper having a deep recess open at the base thereof and closed at the apex thereof such that the apex of the recess is in proximity to the upper surface of the protruding portion,

defining a thin wall portion of the stopper that permits a sharp tip of a syringe needle to be inserted through the thin wall into the upper compartment for withdrawal of the formulation therein; and (ii) a cap assembly that incorporates said actuating means, wherein said actuating means is a means for applying hydraulic pressure via the formulation in the upper compartment to the plug, said pressure tending to disengage the plug from the constriction, thereby pushing the plug into the lower compartment to bring the formulation into contact with the gaseous medium in the lower compartment.

3. The article of Claim 2 wherein the means for applying hydraulic pressure comprises a sleeve of the cap assembly that is snugly disposed around and slidingly engaged with the protruding portion of the stopper; and wherein the sealing portion of the stopper is of larger diameter than the protruding portion and defines at the interface therewith an annular shoulder, said sleeve, adjacent to a lower end thereof, being fracturably connected to an annular gripping portion of the cap assembly; said gripping portion surrounding an radially outward projecting rim formed at the open end of the neck and having at the lower edge of the gripping portion a plurality of substantially uniformly spaced projections extending radially inward; said gripping portion comprising an annular plate that overlies the open end of die neck and circumscribes a plate opening of diameter smaller than the neck opening, such that the annular plate projects radially inward to overlap the stopper shoulder and thereby positively retain die stopper in the neck; said sleeve having, on an outer surface thereof, a plurality of parallel and substantially uniformly spaced ramps that extend axially from and converge with the sleeve toward the gripping portion and that function as a locking means for retaining the sleeve in an actuated position; said sleeve being actuatable by depression thereof to break the fracturable connection and engage with the stopper

shoulder to push the stopper downward, thereby creating hydraulic pressure in the upper compartment

4. (previously cancelled)

5. The article of Claim 1 wherein the gaseous medium is air.

6. The article of Claim 1 wherein the at least one oxidative degradation susceptible ingredient present in the formulation comprises a polyoxyethylene chain.

7. The article of Claim 1 wherein the at least one oxidative degradation susceptible ingredient present in the formulation is a polyoxyethylene surfactant.

8. The article of Claim 7 wherein the polyoxyethylene surfactant is a polysorbate.

9. The article of Claim 7 wherein the polyoxyethylene surfactant is polysorbate 80.

10. The article of Claim 9 wherein the polysorbate 80 is present in an amount of about 0.1 to about 10 mg/ml

11. The article of Claim 9 wherein the polysorbate 80 is present in an amount of about 1 to about 5 mg/ml.

12. The article of Claim 1 wherein the drug present in the formulation is of low water solubility.

13. The article of Claim 1 wherein the drug present in the formulation is selected from the group consisting of acetohexamide, acetylsalicylic acid,

alclofenac, allopurinol, atropine, benzthiazide, carprofen, celecoxib, chlordiazepoxide, chlorpromazine, clonidine, codeine, codeine phosphate, codeine sulfate, deracoxib, diacerein, diclofenac, diltiazem, eplerenone, estradiol, etodolac, etoposide, etoricoxib, fenbufen, fenclofenac, fenprofen, fentiazac, flurbiprofen, griseofulvin, haloperidol, ibuprofen, indomethacin, indoprofen, ketoprofen, lorazepam, medroxyprogesterone acetate, megestrol, methoxsalen, methylprednisone, morphine, morphine sulfate, naproxen, nicergoline, nifedipine, niflumic, oxaprozin, oxazepam, oxyphenbutazone, paclitaxel, phenindione, phenobarbital, piroxicam, piiprofen, prednisolone, prednisone, procaine, progesterone, pyrimethamine, rofecoxib, sulfadiazine, sulfemerazine. Sulfisoxazole, sulindac, suprofen, temazepam, tiaprofenic acid, tilomisole, tolmeiic and valdecoxib.

14. The article of Claim 1 wherein the drug present in the formulation is a steroidal drug.

15. The article of Claim 14 wherein the steroidal drug is selected from the group consisting of clostebol, estradiol, exemestane, medroxyprogesterone, methylprednisolone, testosterone and pharmaceutically acceptable esters and salts thereof.

16. The article of Claim 14 wherein the steroidal drug is selected from the group consisting of estradiol cypionate, exemestane and medroxyprogesterone acetate.

17. The article of Claim 14 wherein the steroidal drug is medroxyprogesterone acetate.

18. The article of Claim 17 wherein the medroxyprogesterone acetate is present in an amount of about 10 to about 400 mg/ml.

19. The article of Claim 17 wherein the medroxyprogesterone acetate is present in an amount of about 30 to about 300 mg/ml.

20. The article of Claim 17 wherein the medroxyprogesterone acetate is present in an amount of about 50 to about 200 mg/ml.

21. The article of Claim 17 wherein the formulation comprises:
(a) medroxyprogesterone acetate, 100-200 mg/ml;
(b) polyethylene glycol of molecular weight 3000-4000, 20-40 mg/ml;
(c) polysorbate 80, 2-4 mg/ml;
(d) sodium chloride, 6-12 mg/ml; and
(e) optionally at least one parenterally acceptable preservative, 0.1-5 mg/ml total.

22. The article of Claim 17 wherein the formulation comprises:
(a) medroxyprogesterone acetate, about 150 mg/ml;
(b) polyethylene glycol of molecular weight about 3350, about 30 mg/ml;
(c) polysorbate 80, about 2.5 mg/ml;
(d) sodium chloride, about 9 mg/ml;
(e) methylparaben, about 1.5 mg/ml;
(f) propylparaben, about 0.15 mg/ml; and
(g) water for injection, *q.s.*

23. The article of Claim 17 wherein the formulation comprises, in a volume of about 0.65 ml:
(a) medroxyprogesterone acetate, about 104 mg;
(b) polyethylene glycol of molecular weight about 3350, about 18.7 mg;
(c) polysorbate 80, about 1.95 mg;
(d) sodium chloride, about 5.2 mg;
(e) methylparaben, about 1.04 mg;

(f) propylparaben, about 0.10 mg;

(g) monobasic sodium phosphate monohydrate, about 0.45 mg;

(h) dibasic sodium phosphate dodecahydrate, about 0.38 mg;

(i) L-methionine, about 0.98 mg;

(j) polyvinylpytrolidone K17, about 3.25 mg; and

(k) water for injection, *q.s.*

ix. Evidence Appendix

None

x. Related Proceedings Appendix

None

To the extent necessary, a petition for an extension of time under 37 C.F.R. § 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including the extension of time fees to Deposit Account 16-1445 and please credit any excess fees to such deposit account.

Respectfully submitted,

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